The Examiner has rejected claims 1-9 and 24 under 35 U.S.C. §112, second paragraph for indefiniteness. The Examiner states that claim 1 is unclear as to whether the conditionally active transactivation domain of CHOP is upstream and operably linked to the sequence specific DNA binding domain. Applicants submit that claim 1 has been amended to indicate that the transactivation domain of CHOP is downstream from the sequence-specific DNA binding domain. With respect to the operable linkage of the transactivation domain of CHOP to the sequence-specific DNA binding domain, Applicants submit that no such operable linkage is required and is thus not recited in the claim. Applicants submit that this will be explained in further detail in response to the rejections below.

Applicants accordingly request that, in consideration of the amendment to claim 1 and the reasoning set for the below, the rejection be reconsidered and withdrawn.

Rejection of Claims 1-9 and 24 Under 35 U.S.C. § 112 First Paragraph

Written Description

The Examiner has rejected claims 1-9 and 24 under 35 U.S.C. §112, first paragraph for lack of written description, asserting that the specification and claims to not teach sufficient identifying characteristics or a representative number or species to describe the claimed genus of a sequence-specific DNA binding protein, and a recognition sequence for a DNA binding protein.

The Written Description Guidelines (Fed. Reg. 66, 2001) clearly set forth the requirements for meeting the written description requirement as required by 35 U.S.C. §112, first paragraph, noting that to satisfy the requirements, "a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention". The Guidelines provide an account of the methods for determining the adequacy of written description, and indicates that "the absence of definitions or details for well established terms or procedures should not be the basis of a rejection under 35 U.S.C. §112, 1¶". The Guidelines provide further that there is an "inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary", and that the "description need only describe in detail that which is new or not

conventional". Finally, the Guidelines state that provided that one of skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is nit explicitly described in the specification, then the adequate description requirement is met".

Applicants submit that sequence-specific DNA binding domains were well known in the art at the time the present application was filed. Applicants submit herewith the results from a MEDLINE search using the term "sequence-specific DNA binding protein" showing that well over 200 papers had been published prior to the filing of the present application relating to sequence-specific DNA binding proteins (Exhibit A). With respect to a recognition sequence for a sequence-specific DNA binding protein, Applicants also submit herewith the results from a second MEDLINE search using the terms "recognition sequence" AND DNA AND "binding protein", which show that more than fifty papers had been published prior to the filing of the present application relating to recognition sequences of sequence-specific DNA binding proteins (Exhibit B). Thus, Applicants submit that the level of skill in the art with respect to a sequence-specific DNA binding protein, and recognition sequence therefore was high at the time the present application was filed. For example, Krajewska (*Int. J. Biochem.*, 24: 1885 (1992)) teaches over 40 specific DNA binding proteins involved in regulation of eukaryotic transcription. Singh et al. (*Biotechniques*, 7: 252 (1989); Exhibit D) as well as others teach a number of transcriptional regulatory DNA binding proteins and their specific recognition sequences. Examples of specific sequence-specific DNA binding proteins and their recognition sequences known in the art are reproduced in the table below.

Sequence-specific DNA Binding Protein	**Recognition Sequence**	**Reference**
H_2TG1/NF-κB	GGGGATTCCCC	Singh et al. *Biotechniques*, 7: 252 (1989)
NG-A2 (Oct-2)	ATGCAAT	Singh et al. *Biotechniques*, 7: 252 (1989)
NF-A1 (Oct-1)	ATGCAAT	Singh et al. *Biotechniques*, 7: 252 (1989)
E12	GGCAGGTGG	Singh et al. *Biotechniques*, 7: 252 (1989)
RF-X	CCCCCTAGCAACAG	Singh et al. *Biotechniques*, 7: 252 (1989)
IRF-1	AAGTGA	Singh et al. *Biotechniques*, 7: 252

		(1989)
PRDI-BF	GAGAAGTGAAAGTG	Singh et al. *Biotechniques*, 7: 252 (1989)
Pit-1	GATTACATGAATATTC ATGA	Singh et al. *Biotechniques*, 7: 252 (1989)
MLTF	CACGTGACCG	Singh et al. *Biotechniques*, 7: 252 (1989)
CREB	TGACGTC	Singh et al. *Biotechniques*, 7: 252 (1989)
Zinc finger proteins	GGGGCGGCT	Desjarlais and Berg, *PNAS* 90: 2256 (1992)
Xbp1	GcCTCGA(G/A)G(C/A)g(a /g)	Mai and Breeden, *Mol. Cell. Biol.* 17: 6491 (1997)

In addition, Suzuki and Yagi (1994, *PNAS* 91: 12357l; Exhibit C) teach that, given the structure of a sequence-specific DNA binding protein (The crystal structure of many sequence-specific DNA binding proteins are known in the art; see for example Pabo et al., Science (1990) 247: 1210; Wolberger et al., (1991) Cell 71: 517; Ferre-D Amare et al., (1993) Nature 363: 38; Ellenberger et al., (1992) Cell 71: 1223; Konig et al, (1994) J. Mol. Biol. 233: 139; Ferre-D Amare et al., (1994) EMBO J. 13: 180; Clarke et al., (1991) Science 254: 267; Schwabe et al., (1993) Cell 75: 567; Ominchinski et al., (1993) Science 261: 438; Kissinger et al., (1990) Cell 63: 579; Hegde et al., (1992) Nature 359: 505; Jordan et al., (1988) Science 242: 893; Anderson et al., (1987) Nature 326: 846; Aggarwal et al., (1988) Science 242: 899; Wolberger et al., (1988) Nature 335: 789; Mondragon et al., (1991) J. Mol. Biol. 219: 321; Rodegers et al., (1993) Structure 1: 227; Shultz et al., (1991) Science 253: 1001; Brennan et al., PNAS 87: 8165; Feng et al., (1985) Science 263: 348; Clark et al., (1993) Nature 364: 412.) the consensus DNA recognition sequence may be identified an a reproducible, predictable manner. That is, given a particular DNA binding protein, one of skill in the art, prior to the filing date of the present application could have made an accurate prediction of what particular DNA sequence would be bound by the protein.

Applicants therefore submit that as of the filing date of the present application, the skill and level of knowledge in the art with respect to sequence-specific DNA binding proteins and their recognition sequences was quite high, and that the state of the art at the time the application was filed had established sufficient correlation between the function of a sequence-specific DNA

binding protein and its recognition sequence and the structures of such proteins and recognition sequences. Therefore, according to the Guidelines, Applicants need not disclose each and every detail of the members of the claimed genus. Accordingly, Applicants submit that one of skill in the art could have reasonably concluded that Applicants were in possession of the invention as claimed. Applicants request that the rejection be reconsidered and withdrawn.

Enablement

The Examiner has rejected claims 1-3, 5-9 and 24 under 35 U.S.C. §112, first paragraph for lack of enablement. The Examiner asserts that while the specification provides a working example comprising a stably integrated recombinant nucleic acid construct comprising a reporter gene operably linked to a GAL4 recognition sequence, the specification does not reasonably provide enablement for a cell line comprising a stably integrated recombinant nucleic acid construct comprising a reporter gene operably linked to any sequence specific DNA binding protein and a nucleic acid construct comprising a sequence encoding a fusion protein comprising any sequence specific DNA binding domain and a conditionally active transactivation domain of CHOP. The Examiner has set forth several factors which were considered in making the present rejection. Applicants have addressed each of these factors below.

The nature of the invention

Applicants respectfully submit that the Examiner's explanation of the invention in this section of the rejection evidences a misunderstanding of the present invention, the clarification of which should obviate the remainder of the Examiner's rejection. The Examiner asserts that the claimed invention relies on a nucleic acid construct comprising a sequence encoding a fusion protein comprising a sequence specific DNA binding domain operably linked and downstream of the conditionally active transactivation domain of CHOP, *whereby the transactivation of the CHOP domain leads to increased expression of the sequence specific DNA binding domain*, which subsequently binds the corresponding recognition sequence that is operably linked and upstream of the reporter gene thereby leading to increased reporter gene expression.

Applicants respectfully submit that the Examiner's characterization of the invention is incorrect. The invention relates to a cell line comprising, in part, a stably integrated nucleic acid

construct comprising a sequence encoding a fusion protein, which comprises a sequence-specific DNA binding domain and a conditionally active transactivation domain of CHOP. The sequence encoding the sequence-specific DNA binding domain and the sequence encoding the conditionally active transactivation domain of CHOP are expressed from a single promoter as shown in Figure 5. That is, as shown in Figure 5, activation of the CMV promoter results in the transcription of **both** the sequence-specific DNA binding domain and the sequence encoding the conditionally active transactivation domain of CHOP to produce a fusion protein., The specification teaches at page 27, that the sequence-specific DNA binding domain/conditionally active transactivation domain of CHOP construct is operably linked to an appropriate, preferably eukaryotic promoter, such as a viral control sequence, promoters for eukaryotic cellular genes, housekeeping gene promoters, or even tissue-specific promoters. Thus, the stably integrated construct encoding the sequence-specific DNA binding protein and the conditionally active transactivation domain of CHOP is constitutively expressed under the control of a promoter functional in the claimed cell line. Unlike the Examiner's characterization, it is not the expression and activation of CHOP which leads to increased expression of the sequence specific DNA binding domain, **both** the sequence-specific DNA binding domain and the transactivation domain are **expressed together as a fusion protein**. It is the fusion protein which then is able to bind, via the sequence-specific DNA binding domain to the recognition sequence for a sequence-specific DNA binding protein linked to the reporter gene.

With respect to the orientation of the fusion protein, Applicants have amended claim 1 to indicate that the sequence-specific DNA binding domain is upstream of the CHOP transactivation domain. Applicants submit that unlike the Examiner's assertion, however, the orientation of the sequence-specific DNA binding domain and the transactivation domain is irrelevant for the purpose of forming the fusion protein to begin with. That is, the expression of the sequence-specific DNA binding domain is not dependant on the expression and transactivation of the CHOP transactivation domain.

<u>The amount of direction or guidance presented in the specification and the presence or absence of working examples</u>

The Examiner asserts that Applicants have not provided guidance for the generation of stable cell lines comprising a stably integrated recombinant nucleic acid comprising a reporter gene operably linked to a recognition sequence for any and/or all sequence specific DNA binding proteins, nor for the transactivation of a reporter gene following binding of any and/or all sequence specific DNA binding proteins to their corresponding recognition sequences, nor for the transactivation or increased expression of a reporter gene following activation of the transactivation domain of CHOP which is located downstream of a sequence specific DNA binding protein. Applicants respectfully disagree.

Applicants submit that the legal standard on which the enablement requirement is based hinges on a determination of whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. As stated in *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ 2d 1217 (Fed. Cir. 1988), *cert denied*, 490 U.S. 1046 (1989), the court reversed the findings of the district court of undue experimentation where the specification provided only one working example. "The court ruled that since one embodiment (stainless steel electrodes) and the method to determine dose/response was set forth in the specification, the specification was enabling. The question of time and cost of such studies...failed to show undue experimentation." MPEP 2164.06 further points to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-504, 190 USPQ 214, 217-19 (CCPA 1976)), which states:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

In addition, in *Ex parte Mark,* 12 U.S.P.Q.2D 1904 (BPAI, 1989) the court determined that Appellants' invention was enabled given that the specification taught substituting a nonessential cysteine with a neutral amino acid, wherein the nonessential cysteine residues of any candidate protein could then be identified and substituted in ten days employing the methods disclosed in the instant disclosure and the general knowledge of the art at the time the application was filed. The court ruled that:

> The fact that a given protein may not be amenable for use in the present invention in that the cysteine residues are needed for the biological activity of the protein does not militate against a conclusion of enablement. One skilled in the art is clearly enabled to perform such work as needed to determine whether the cysteine residues of a given protein are needed for retention of biological activity.

Thus, the specification need only provide a teaching of how to make and use the present invention sufficient to enable one of skill in the art to practice the invention without undue experimentation. The law does not require Applicants to disclose a working example for every embodiment of the invention (or any embodiment, for that matter). *Ex parte Mark*, 12 U.S.P.Q.2d 1904 (Bd. Pat. App. & Int. 1989). Applicants further submit that they are not required to teach that which is already well known in the art. *In re Buchner*, 929 F.2d 660 (Fed. Cir. 1991).

Applicants submit that in order to meet the enablement requirement as set forth in 35 U.S.C. §112, first paragraph, they must teach (1) how to construct an recombinant nucleic acid construct comprising a reporter gene operably linked to a recognition sequence for a sequence-specific DNA binding protein; (2) how to construct a stably integrated recombinant nucleic acid construct comprising (a) a sequence encoding a fusion protein comprising a sequence-specific DNA binding domain which binds to the recognition sequence and (b) a conditionally active transactivation domain of CHOP; and (3) how to incorporate the two nucleic acid constructs into a host cell such that the constructs become stably integrated. Applicants submit that the specification adequately teaches each of these aspects of the present invention so as to permit one of skill in the art to reproduce the invention as claimed without undue experimentation. Applicants submit that the specification provides the following teachings:

> Pages 18-19, and 24-26 teach the sequence of a transactivation domain of CHOP which may be used in the present invention

> Page 20 teaches reporter cell lines, including HeLa cells which may be stably transfected with the nucleic acid constructs of the invention.

Pages 20-23, and 36-45 teach reporter genes, methods for including such genes in an expression plasmid along with a recognition sequence for a sequence specific DNA binding domain, and assays for measuring their expression.

Pages 23-24 teach sequence specific DNA binding domains useful in the invention.

Pages 26-28 teach how to construct a sequence-specific DNA binding domain/transactivation domain expression plasmid, including promoters, enhancers, and selectable markers useful in the invention.

Pages 28-31, and 36-45 teach methods for generating stably transfected cells and methods for determining the stability of integration.

In addition, the specification, at pages 45-50, provides a working example demonstrating the operability of the present invention using the sequence-specific DNA binding domain and recognition sequence for GAL4. As described above, the level of skill and knowledge in the art relating to sequence-specific DNA binding proteins and their recognition sequences was quite high as of the filing date of the present application. Accordingly, Applicants submit that one of skill in the art, given the teachings of the present specification, in combination with the well-established knowledge in the art, would be capable of reproducing the present invention to the extent claimed without undue experimentation.

The Examiner asserts that one of skill in the art would not accept on its face the examples given in the specification of the operability of the present invention, as being correlative or representative of cell lines comprising any sequence specific DNA binding protein and any corresponding recognition sequence. Applicants disagree. The specification teaches that the function of the sequence-specific DNA binding protein and cognate recognition sequence is to bring the CHOP transactivation domain into close spatial proximity to the reporter gene so as to permit transactivation of reporter gene expression by CHOP. As noted above, at the time the present application was filed, one of skill in the art was well versed in the properties of DNA binding domains and their cognate recognition sequence. Applicants respectfully inquire why the Examiner doubts that one of skill in the art, given the knowledge in the art and Applicants'

teachings, could have selected a sequence-specific DNA binding protein and its known recognition sequence (e.g., a DNA binding protein other than GAL4 or LexA, such as a zinc finger binding protein, or Xbp-1) and, following the teachings of the present invention, included each sequence respectively in an expression construct with a transactivation domain of CHOP, and an expression construct with a reporter gene.

The Examiner further asserts that the specification fails to provide any particular guidance which resolves the known unpredictability in the art associated with the ability to construct recombinant nucleic acid comprising a reporter system which utilizes any and/or all sequence specific DNA binding domains and their corresponding recognition sequences. Applicants respectfully request clarification as to what "known unpredictability" the Examiner is referring to. As set forth in *In re Wright*, the Examiner bears the burden of establishing a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993). Applicants submit that the Examiner has not met this burden. Applicants further submit that, in view of the teachings in the specification, actual working examples of the present invention, demonstrating that the invention is operable as claimed, and in further view of the level of knowledge in the art with respect to sequence-specific DNA binding proteins and their recognition sequences, there is no reasonable basis for questioning the enablement provided for the claimed invention.

The breadth of the claims and the quantity of experimentation required

The Examiner asserts further that it would require undue trial and error and undue experimentation beyond which is taught in the specification to practice the invention drawn to nucleic acid constructs comprising any and/or all sequence specific DNA binding domains and their corresponding recognition sequences. The Examiner further asserts that practice of the claimed invention would require the *de novo* determination of a representative number of species in the broad genus comprising nucleic acids encoding any and/or all sequence specific DNA binding domains and their corresponding recognition sequences. Applicants respectfully disagree.

Applicants submit that they have met the burden of enablement which is clearly established by law; that is, they have taught how to make and use the invention as claimed

without undue experimentation. As the Examiner is no doubt aware, even a large amount of experimentation is permissible, provided that it is not undue. Applicants submit that the Examiner's characterization of the nature of the experimentation necessary to perform the invention as claimed is incorrect. Practice of the invention would not require the "*de novo* determination of a representative number of species in the broad genus". Applicants submit that a representative number of species in the broad genus was already known in the art when the application was filed, and as stated above, Applicants are not required to re-teach that which is in the prior art. Applicants submit that with nominal experimentation, one of skill in the art could have selected a sequence-specific DNA binding protein and a corresponding recognition from the plethora of such molecules known in the art, and used them in accordance with the teachings of the present invention to practice the claims to their full scope.

Applicants accordingly submit that the present claims are enabled as written and request that the Examiner reconsider and withdraw the rejection.

Rejection of Claims 1-7 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-7 under 35 U.S.C. §102(b) as being anticipated by Wang et al., (1996, Science 272: 1347). The Examiner asserts that Wang teach stably transfected mammalian cells comprising a constitutively expressed fusion construct comprising the conditionally active transactivation domain of CHOP operably linked to a GAL4 DNA binding domain, and which stably transfected cells further comprise a reporter plasmid comprising the luciferase gene operably linked to the GAL4 recognition sequence. Applicants respectfully disagree.

Wang does not describe or disclose a cell line comprising stably integrated recombinant nucleic acid constructs. Stably transfected cells are known in the art to require negative selection to eliminate cells which have been succesfully transfected, but in which the transfected construct has not been integrated into the host cell chromosome (See, for example Ausubel et al. Short Protocols in Molecular Biology, 4th Ed. 1999, John Wiley and Sons, Inc., New York). Accordingly, "stably integrated" has been defined in the present specification as the "incorporation of a nucleic acid construct into the genome of a host cell such that it is replicated when the genome is replicated and passed onto the progeny cells upon cell division for at least

two cell divisions" (page 11, lines 13-15). In contrast, Wang does not teach negative selection of transfected cells to eliminate cells which have been only transiently transfected, or the replication of a nucleic acid construct for at least two cell divisions, and moreover, provides no descriptive indication that would confirm or even suggest to one of skill in the art that the disclosed NIH-3T3 cells are stably transfected. The only teaching in Wang of stably transfected cells is in the legend for Figure 3D, in which the cells are specifically referred to as stably transfected, but which does not, however, relate to measuring CHOP transactivation, but instead relates to the differentiation of 3T3-L1 cells into adipocytes.

Accordingly, Applicants submit that Wang does not teach cells lines comprising stably integrated recombinant nucleic acid as required by the claims of the present invention, and thus does not anticipate the present invention.

Applicants therefore request that the rejection be reconsidered and withdrawn.

Rejection of Claims 1-9 and 24 Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-9 and 24 under 35 U.S.C. §103(a) as being obvious over Wang et al., in view of Lin et al., (1995, Science, 268: 286) and Wieder et al., U.S. Pat. No. 5,620,881. The Examiner asserts that Wang teach stably transfected NIH-3T3 cells, but not stably transfected HeLa cells. The Examiner further asserts that Lin teach the participation and interactions of various kinase cascades in cellular growth and differentiation including p38, which is a known activator of CHOP, in various cell lines including HeLa cells, and that Wieder teach the stable transfection of fibroblast derived cells including HeLa cells. Applicants respectfully disagree with the Examiner.

For the reasons described below, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness under the requirements of 35 U.S.C. § 103(a). To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings (In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)). Second, there must be a reasonable expectation of success. The teaching or suggestion to make

the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

Applicants submit that there is no motivation to combine the teachings of the references cited by the Examiner. As described above, Wang do not teach stably transfected cells, but, in fact, teach transiently transfected cells. There is no teaching in either Lin or Wieder which would motivate one of skill in the art to modify the teachings of Wang to produce stably transfected HeLa cells. Kinase cascades have been studied *in vivo*, *in vitro*, and in myriad cell types and cell lines. The mere teaching in Lin that the p38/MAPK cascade exists in HeLa cells, given that this cascade functions in many different mammalian cells, is by no means sufficient to motivate one of skill in the art to look to modify the teachings of Wang by adopting a new model cell system. One of skill in the art would have been no more motivated to combine the teachings of Wang with those of Wieder to generate stably transfected HeLa cells. Applicants submit that Wieder do teach stable transfection of HeLa cells, however, Wieder is drawn primarily to the study of the immune system in response to the HIV infection. That is, there is no teaching in Wieder that one of skill in the art should or could look to stably transfected HeLa cells as a model system for the assessment of signal transduction cascades such as the p38/MAPK cascade. Further, there is no teaching in either Wang or Lin that would motivate one of skill in the art to seek out a method for stably transfecting cells with components of the p38/MAPK/CHOP pathway, given that both of these references teach that this pathway can be assayed in transiently transfected cells. Applicants submit that the teaching of stable transfection of HeLa cells for purposes of studying immune responses is by no means sufficient to motivate one of skill in the art to stably transfect HeLa cells for the study of any other biological phenomena, such as activation of CHOP transactivation.

In addition, applicants submit that one of skill in the art, given the teachings of Wang, Lin and Wieder would not have expected success in the stable transfection of HeLa cells for the study of CHOP dependant signal transduction. As noted above, Wang teach that CHOP-dependent signal transduction may be studied in NIH-3T3 cells. It is well known in the art, however, that signal transduction systems do not function the same in all cell types, and that

proteins involved in such cascades are not functionally identical across all cell types. Thus, the teaching in Lin that the p38 system functions in HeLa cells does not, absent teaching otherwise, permit the assumption that p38 will act on the CHOP pathway in HeLa cells in the same manner in which it does in NIH-3T3 cells. Thus, there is no teaching in either Wang or Lin to suggest to one of skill in the art that a successful examination of CHOP transactivation may be performed in HeLa cells, whether they are stably transfected or not.

Accordingly, Applicants submit that the present invention is non-obvious over the teachings of Wang, Lin, and Wieder, taken alone or in combination. Applicants therefore request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date: January 16, 2003

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Marked-up Version of Amendment

Please **replace** claim 1 with the following claim:

1. (Amended) A cell line comprising a stably integrated recombinant nucleic acid construct comprising: a reporter gene operably linked to a recognition sequence for a sequence-specific DNA-binding protein; and a stably integrated recombinant nucleic acid construct comprising a sequence encoding a fusion protein, said fusion protein comprising a sequence-specific DNA binding domain, wherein said DNA binding domain specifically binds said recognition sequence, and a conditionally active transactivation domain of CHOP, wherein binding of said fusion protein to said recognition sequence results in transactivation of said reporter gene when said transactivation domain fused to said DNA binding domain is activated, and wherein said sequence-specific DNA binding domain of said fusion protein is located upstream of said conditionally active transactivation domain of CHOP.